REMARKS

Claim status

Claims 52-54 and 106-108 are pending. By this amendment, claims 52-53 and 106 have been amended. New claims 113-123 have been added. Support for the new claims can be found in the specification as follows:

Claim **113**: Example 3, page 11, lines 10-11; page 12, lines 8-10, and Table I, column 2; page 13, Table III, column 2.

Claims **114, 115,** and **120**: Example 1, page 11, lines 2-3; page 12, lines 8-10, and Table I, column 3; page 13, Table III, column 3; Example 4, page 15, line 11.

Claim **116**: Page 7, lines 18-19; page 15, lines 20-22; page 9, lines 17-19 and 20-22. .

Claim **117**: Page 13, lines 1-2.

Claims **118** and **119**: Original claim 1 and claim 106.

Claim **120**: Example 1, pp. 9-11; and Example 3, page 12.

Claim **121** and **122**: Example 1 pages 9-11, total mixture produced is 12,495 g. Percents of each component ingredient are divided. For example, 1000 g of micronized progesterone is 8% of a total of 12,495 g.

Upon entry of this amendment, claims 52-54 and 106-123 will be pending and under examination.

Interview Summary

Applicants thank the Examiner for the courtesies extended during the in-person interview conducted on November 7, 2005, in Examiner Pryor's office. Present at the interview was Examiner Pryor, Dr. Jakob Poulsen, in house patent counsel for the Assignee, and Applicant's agent of record, Dr. Stephanie Amoroso.

Prior to the interview, claims 52-54 and 106-108 were rejected as being obvious over U.S. Patent 5,084,277 to Greco, in view of U.S. Patent 4,853,211 to Kurobe. During the interview, the cited prior art of record (U.S. 5,084,277 to Greco, and U.S. 4,853,211 to Kurobe), and U.S. 5,958,455 to Roser (a prior art reference of record in co-pending, commonly-owned application serial number 10/832,742) were discussed in view of the pending claims of record (pursuant to the Response filed on April 4, 2005).

To expedite prosecution, it was agreed that claim 52 would be amended to recite that the tablet "consists essentially of" progesterone as the active ingredient. This amendments renders the claim open for the inclusion of only unspecified ingredients that do not "materially affect the basic and novel characteristics of the claimed composition." *Dow Chemical Co. v. American Cyanamid Co.*, 615 F.Supp. at 484, 229 USPQ at 180. It also was agreed during the interview that this language should not operate to close the claim to excipients or diluents that are not active ingredients. Claim 52 is herein amended to recite a method of delivering progesterone to a female patient, comprising placing in the vagina of said patient a tablet consisting essentially of progesterone as the active ingredient, pharmaceutically acceptable excipients or diluents, and an effervescent, and retaining said tablet in the vagina for a time efficacious to deliver progesterone to said patient.

Regarding the term "as the active ingredient," it would be clear to one of ordinary skill in the art from reading the specification that progesterone is the only ingredient disclosed that is an active ingredient (i.e., drug). It is well-established law that the specification does not have to

provide *in haec verba* support (exact words) for the claimed subject matter at issue as long as one of ordinary skill in the art would discern the limitation from the disclosure. *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 56 USPQ2d 1481 (Fed. Cir. 2000). See also *Union Oil of California v. Atlantic Richfield Co.*, 208 F.3d 989, 54 USPQ2d 1277 (Fed. Cir. 2000) (The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, instead the description must clearly allow persons of ordinary skill in the art to recognized that the inventor had possession of the claimed invention). The MPEP also states that there is no *in haec verba* requirement for claim limitations, but they can be implicit or inherent (MPEP 2163 IB)

Second, there is clear an unambiguous support in the specification and originally filed claims for the term "pharmaceutically acceptable excipients or diluents." See page 4, lines 11 and 14-15; page 8, lines 11 and 23; and original **claims** 1-3 of the application-PCT WO00/28970). According to MPEP, lack of written description for an original claim should be **rare** (see MPEP 2163 II.A).

In addition, the specification at pages 9 and 11 lists several pharmaceutically acceptable excipients or diluents (colloidal anhydrous silica, maize starch, lactose, povidone, magnesium stearate, and sodium lauryl sulfate) that can be present in the tablet. These agents are specifically recited in new claims 122-123.

Accordingly, claim 52, as amended embraces the addition of more than one pharmaceutically acceptable excipient or diluent. New independent claims 121 and 122 also contain the agreed upon "consisting essentially of" language. As such it s presumed these claims are also allowable.

Greco-5,084,277

During the interview, the Examiner agreed that Greco teaches away from using an effervescent in his vaginal progesterone tablet. Specifically, at column 5, lines 41-51, Greco teaches that use of an effervescent is to be avoided because of the following:

> Although ..."super disintegrants" can explode tablets very quickly in moist environments such as the mouth, the present inventors have determined that super disintegrants in a vaginal tablet turn the tablet into a sponge-like mass following vaginal insertion. A milky suspension is not formed , and drug absorption is regarded. Smaller amounts of the super disintegrants cause a gelatinous sheath to form around the tablet, which inhibits further tablet disintegration and thereby reduces drug bioavailability.

In addition to the foregoing negative teaching, those skilled in the art would not be motivated to use an effervescent in Greco's tablet because Greco's tablet provides a T_{max} (time to peak plasma concentration of progesterone) of 23.3 hours (column 11, lines 35-36). The presence of an effervescent in Greco's tablet would be highly detrimental this "sustained release" property, since effervescents enhance tablet dissolution and absorption. By contrast, as disclosed in the present specification, the tablet administered according to the presently claimed method provides a T_{max} of between about 3 and about 10 hours (see Table V on page 15, and lines 11-14 on page 15). This is much shorter than the 23.3 hours of Greco's tablet, and is due to the presence of the effervescent which expedites dissolution (and hence, absorption) of progesterone.

During the interview, it was also pointed out that Greco actually teaches away from the presence of an effervescent since his tablet is prepared by wet granulation. During the wet granulation, any effervescent would react with the water used for the wetting and would not be available in the final product.

In view of the foregoing, it was agreed that Greco does not render the present claims obvious over Greco.

Lastly, it is well established law that the proposed combination cannot render the prior art unsatisfactory for its intended purpose. *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984) and MPEP 2143.01. If the proposed combination of references would change the principle of operation of the prior art invention being modified, then the references are not sufficient to render the claims obvious (*In re Ratti*, 270 F.2d 819; MPEP 2143.01). As demonstrated above, the addition of an effervescent to Greco's tablet would render it unsuitable to provide a sustained release of progesterone as intended.

Kurobe-5,853,211

During the interview it was also agreed that U.S. Patent 4,853,211 to Kurobe did not teach or suggest use of a vaginal progesterone tablet as presently claimed. It was pointed out that Kurobe teaches a vaginal suppository formulation containing a **contraceptive**. This is in contrast to the progesterone tablet used in the method of the present claims. Dr. Amoroso asserted, and the Examiner agreed, that progesterone is not used for vaginal contraception, but is instead used for the opposite purpose of promoting and supporting pregnancy. It was also agreed that it is well understood that vaginally administered progesterone is used for promoting and supporting pregnancy, such as during assisted reproduction, and is **not** for contraception. The disclosure in the Greco patent (column 1, lines 14-16) supports the position that one of ordinary skill in the art recognizes that vaginally administered progesterone is used to promote pregnancy, and not to prevent pregnancy:

> The major biologic functions of progesterone are to prepare the uterine endometrium for fertilization and implantation and to support pregnancy.

The differences between a suppository formulation, such as that taught by Kurobe, and a tablet formulation as called for by the present claims also were discussed. The agent for the Applicant conveyed the importance of being able to vaginally deliver and have absorbed precise

doses of progesterone during assisted reproduction, in order to provide consistent blood levels of progesterone. It was pointed out that the use of progesterone suppositories is not preferred for this purpose, since suppositories melt at body temperature and create leakage and discharge from the vagina. This results in loss of progesterone and reduced absorption by the patient. It was further indicated that use of a vaginal tablet avoids the leakage and discharge associated with a suppository formulation. Lastly, it was pointed out that inclusion of an effervescent in the tablet aids dissolution of the tablet and further increases absorption of the progesterone without excessive loss of progesterone.

Accordingly, it was agreed that Kurobe teaches away from the progesterone tablet disclosed in the Greco patent, and also teaches away from the tablet used in the presently claimed method.

Moreover, as indicated above the proposed combination cannot render the prior art unsatisfactory for its intended purpose. *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984) and MPEP 2143.01. If the proposed combination of the references would change the principle of operation of the prior art invention being modified, then the references are not sufficient to render the claims obvious (*In re Ratti*, 270 F.2d 819; MPEP 2143.01). As demonstrated above, the addition of progesterone to Kurobe's tablet would render it unsuitable for contraception, since progesterone is used to enhance the likelihood of pregnancy.

Roser-5,958,455

Lastly, it was also agreed at the interview that U.S. 5,958,455 to Roser teaches away from the tablet used in the presently claimed method. First, Roser teaches a rapidly-dissolving tablet for **oral**, not **vaginal** administration.

In addition, Roser explicitly teaches away from using an effervescent in the disclosed tablet at column 13 line 65, to column 14, line 3:

> The production of rapidly dissolving tablets was again achieved by the addition of a volatile salt to the tableting blend, followed by **removal of the salt under vacuum** to obtain a porous tablet that showed increased dissolution rates compared to tablets of the same blends without the volatile salt incorporated (emphasis supplied).

In addition, at column 14, lines 59-61, Roser states that:

> The results presented in Table 2 indicate that **removal of volatile salt** to give porous tablets significantly increased the disintegration and dissolution rates of the tablets produced (emphasis added).

In other words, Roser includes an effervescent (i.e., volatile salt) during the tableting process to make a porous matrix, but the efferscent is completely removed from the final product. According to Table 2, at column 14, the volatile salt that is completely removed from the final tablet is ammonium bicarbonate, a well-known effervescent.

Further, Examiner Pryor was informed that Roser discloses the presence of an effervescent in the background section of his patent, in the context of an oral tablet that is pre-dissolved in water first (see column 2, lines 7-13). Examiner Pryor agreed that an effervescent tablet that must first be pre-dissolved in water would not be suitable for vaginal administration.

Moreover, as indicated above, the proposed combination cannot render the prior art unsatisfactory for its intended purpose. *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984) and MPEP 2143.01. If the proposed combination of the references would change the principle of operation of the prior art invention being modified, then the references are not sufficient to render the claims obvious (*In re Ratti*, 270 F.2d 819; MPEP 2143.01). As demonstrated above, the addition of an effervescent to Kurobe's tablet would render it unsuitable, since Kurobe makes it clear that the effervescent is **removed** during tableting.

Claim 106

Claim 106 was not discussed during the interview. This claim is directed to a method of delivering progesterone to a female in a tablet, where the tablet is prepared by a method recited in the claims.

Claim 106 as written excludes the presence of any other ingredient "that materially effects the basic and novel characteristics of the claimed composition," since the recited steps do not permit for addition of another active ingredient. However should the Examiner (or whomever is actually in a position to allow this case) disagree, the it is respectfully requested that he call the undersigned agent of record to discuss potential amendments to make this clear.

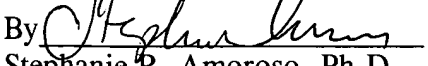
Conclusion

To expedite prosecution, Applicants agreed to amend claim 52 to recite "consisting essentially of" in response to the Examiner's suggestion (in view of Quality assurance review). However, since it was agreed during the interview that none of the cited references renders the present claims obvious, this amendment is **not** necessary for patentability.

In view of the above amendments made pursuant to the in person interview, Applicants believe the pending application is in condition for allowance.

Dated: November 28, 2005

Respectfully submitted,

By 

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